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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,663	09/19/2001	David M. Roche	19629-7006	1221

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EXAMINER

LY, CHEYNE D

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 03/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/955,663

Applicant(s)

ROCKE ET AL.

Examiner

Cheyne D. Ly

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-8 and 10 is/are rejected.
- 7) ☒ Claim(s) 9, 11 and 12 is/are objected to.
- 8) ☒ Claim(s) 2-12 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicants' arguments filed December 23, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
3. Claims 2-12, nucleic acid molecule, are examined on the merits.

### **LACK OF ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH**

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:  
  
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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6. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.
7. Claim 3, (c), and claim 4, (c), recite the limitation of “c” wherein c is in the range of 2 and 3. However, the claims do not recite any limitations which define the variable “c”. Further, the specification on page 11 recites a step for calculating “c=2, 2.5, or 3.” However, the instant specification does not provide any direction by guidance or working examples as to how the value for “c” has been determined to be used in the claimed method. Therefore, one of skill in the art would not be able to predictably practice the claimed invention without undue experimentation.

#### CLAIM REJECTIONS - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
10. Claims 2, 5-8, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rocke et al. (1995) taken with Bailey et al. (1987).
11. It is noted that the specification describes the applications of a plurality of thresholding algorithms (page 12-13). However, the limitation of "a thresholding algorithm" in claim 2, lines 15-16, is not specific to any thresholding algorithm. Therefore, the "thresholding algorithm" limitation is not limited to any specific "thresholding algorithm." The "thresholding algorithm" limitation has been reasonably interpreted as any algorithm which establishes a cutoff and the set of low-level data consists of those data with values less than the cutoff.

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12.     Rocke et al. discloses a method for estimating the precision measurements of biological samples (page 176, column 1, lines 25-30) using the estimated variance of equation 3.3 for low and high levels of the data measurements (page 179, column 1, §3.2; and Figure 4), as in instant claim 2, steps (a), (d), (f), and (g).
13.     The method of Rocke et al. comprises a matrix (array) wherein data is derived from analyzing blanks (background parameter), additive error components (page 176, column 2, lines 16-18 and page 177, §2, lines 2-4), and standard deviation of data measurements (page 177, column 2, lines 6-8), as in instant claim 2, steps (b), (c), and (e).
14.     Rocke et al. discloses the new model more clearly demonstrates the usefulness of measurements below quantitation levels (page 177, column 2, lines 27-32). The analysis of Cadmium by atomic absorption spectroscopy uses the algorithms from section 3.2 to establish confidence levels (thresholds). An absorbance of 6 implies an estimated concentration of 2.75 ppb, with 95% confidence interval (2.47, 3.004). The absorbance of 50 implies an estimated concentration of 21.76 ppb, with 95% confidence interval (20.69, 22.88). The estimated concentration of 2.75 ppb has been reasonably interpreted as less than the cutoff of 3.004 (page 181, column 1, line 29, to column 2, line 12), as in instant claim 2, lines 15-17.
15.     “For low levels, the average of n measurements will be approximately normally distributed with standard deviation” (page 179, column 1, §3.3). “As an example, suppose

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$\sigma_s = 1$  part per billion (ppb) and  $\sigma_n = .1$ . Then the standard deviation of blanks (negative control and background) is 1 ppb (page 177, column 2, lines 5-8), as in instant claims 5-7.

16. However, Rocke et al. does not disclose the limitation of biological molecule is a nucleic acid.

17. The method of Rocke et al. is directed to GC-MS analysis (page 177, column 1, lines 6-11).

18. Bailey et al. discloses a method for estimating exposure to alkylating carcinogens GC-MS determination of adducts in DNA (Abstract etc.), as in instant claims 8 and 10.

19. The method of Bailey et al. is an improvement for increasing the sensitivity of dosimetry by overcoming the presences of background levels (page 190, column 1, Conclusions §).

20. Rocke et al. discloses a method for measuring near the detection limit (page 176, column 1, §1) as applied to environmental monitoring for low levels of toxic substances (page 178, column 2, §3). The improvement described by Rocke et al. is to provide an easy way to give precise measurements (page 177, column 2, lines 27-32).

21. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement disclosed by Bailey et al. to utilize said improvement with the

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method of Rocke et al. for environmental monitoring for low levels of toxic substances.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use a method of environmental monitoring for low levels of toxic substances as taught by Rocke et al. and Bailey et al.

22. It is noted that the Rocke et al. and Bailey et al. references have been previously provided; therefore, said references are not provided with the instant office action.

### CONCLUSION

23. Claims 9, 11, and 12 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
24. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. The USPTO's official fax number is (571) 273-8300.
25. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic



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26. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.
27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.
28. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

C. Dune Ly  
3/1/05

 3/1/05  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER